Claims:

The following listing of claims will replace all prior versions and listings of claims in the application:

1. (Currently Amended) A pharmaceutical formulation for pulmonary administration as a powder, the pharmaceutical formulation comprising:

particulates ~~comprising~~ consisting essentially of ~~an~~ active agent ~~particle~~ particles in a phospholipid ~~lipid~~ matrix, ~~the active agent having a solubility in water of less than 1.0 mg/ml;~~ wherein the active agent particles are dispersed throughout the phospholipid matrix; and

wherein at least 90% of the active agent particles ~~in the pharmaceutical formulation~~ have a geometric diameter less than 3 μm and wherein the particulates have a mass median diameter less than 10 ~~20~~ μm and a bulk density of less than about 0.5 g/cm^3.

2. (Currently Amended) A pharmaceutical formulation according to claim 1 wherein the particulates have a mass median aerodynamic diameter less than ~~10 μm~~ about 2.6 μm.

3. (Currently Amended) A pharmaceutical formulation according to claim 1 wherein ~~the particulates have a mass median diameter less than 5 μm~~ a formulation emitted dose is at least about 93 percent.

4. (Currently Amended) A pharmaceutical formulation according to claim 1 wherein ~~at least 95% of the active agent particles have a geometric diameter less than 3 μm~~ a formulation fine particle fraction of less than 3.3 μm is at least about 72 percent.

5. (Currently Amended) A pharmaceutical formulation according to claim 1 wherein ~~at least 50% of the active agent particles have a geometric diameter between 0.5 μm and 3 μm~~ the formulation exhibits an Ostwald ripening as depicted in Fig 1.

6. (Currently Amended) A pharmaceutical formulation according to claim 1 wherein ~~at least 50% of the active agent particles have a geometric diameter between 1 μm and 3 μm~~ the formulation provides for the delivery to the lung of a dose of at least about 5 mg in a single inhalation.

7. (Original) A pharmaceutical formulation according to claim 1 wherein the lipid matrix comprises one or more phospholipids.

8. (Currently Amended) A pharmaceutical formulation according to claim 1 wherein the ~~lipid~~ matrix comprises one or more of dipalmitoylphosphatidylcholine, ~~distearoylphosphatidylcholine~~ distearoylphosphatidylcholine, diarachidoylphosphatidylcholine dibehenoylphosphatidylcholine, diphosphatidyl glycerol, short-chain phosphatidylcholines, long-chain saturated phosphatidylethanolamines, long-chain saturated phosphatidylserines, long-chain saturated phosphatidylglycerols, and long-chain saturated phosphatidylinositols.

9. (Original) A pharmaceutical formulation according to claim 1 wherein the particulates are hollow.

10. (Original) A pharmaceutical formulation according to claim 1 wherein the particulates are porous.

11. (Original) A pharmaceutical formulation according to claim 1 wherein the particulates are hollow and porous.

12. (Currently Amended) A pharmaceutical formulation according to claim 1 wherein ~~the pharmaceutical formulation has a bulk density of less than 0.5 g/cm^3~~ the active agent comprises tobramycin.

13. (Original) A pharmaceutical formulation according to claim 1 wherein the pharmaceutical formulation has a bulk density of less than 0.3 g/cm^3.

14. (Original) A pharmaceutical formulation according to claim 1 wherein the pharmaceutical formulation has a bulk density of less than 0.2 g/cm^3.

15. (Original) A pharmaceutical formulation according to claim 1 wherein the particulates are in dry powder form for aerosolization in a dry powder inhaler.

16. (Original) A pharmaceutical formulation according to claim 1 wherein the particulates are suspended in a propellant for aerosolization in a metered dose inhaler.

17. (Original) A pharmaceutical formulation according to claim 1 wherein the particulates are suspended within a liquid for aerosolization in a nebulizer.

18. (Original) A pharmaceutical formulation according to claim 1 wherein the active agent particle is crystalline.

19. (Original) A pharmaceutical formulation according to claim 1 wherein the particulate further comprises a polyvalent cation.

20. (Currently Amended) A pharmaceutical formulation according to claim 1 wherein the active agent has a solubility in water of less than [[0.1]] 1.0 mg/ml.

21. (Currently Amended). A pharmaceutical formulation according to claim 1 wherein the particulates are formed by spray drying with a blowing agent.

22. (Original) A pharmaceutical formulation according to claim 1 wherein the insoluble active agent comprises an antimycotic agent.

23. (Withdrawn) A method of making a pharmaceutical formulation for pulmonary administration, the method comprising: suspending active agent particles and a hydrophobic material in a liquid feedstock, wherein at least 90% of the active agent particles have a geometric diameter less than 3 μm; and spray drying the feedstock suspension to produce particulates comprising an active agent particle at least partially in the hydrophobic material.

24. (Withdrawn) A method according to claim 23 wherein the feedstock comprises water and wherein the active agent has a solubility in water of less than 1.0 mg/ml.

25. (Withdrawn) A method according to claim 23 further comprising collecting the particulates.

26. (Withdrawn) A method according to claim 25 wherein the collected particulates have a mass median diameter less than 20 μm.

27. (Withdrawn) A method according to claim 25 wherein the collected particulates have a mass median diameter less than 10 μm.

28. (Withdrawn) A method according to claim 23 wherein 95% of the active agent particles have a geometric diameter less than 3 μm.

29. (Withdrawn) A method according to claim 23 wherein the hydrophobic material comprises a lipid.

30. (Withdrawn) A method according to claim 23 wherein the hydrophobic material comprises a phospholipid.

31. (Withdrawn) A method according to claim 23 wherein the hydrophobic material comprises a hydrophobic amino acid.

32. (Withdrawn) A method according to claim 23 further comprising adding an emulsifying agent to the feedstock.

33. (Withdrawn) A method according to claim 23 wherein the emulsifying agent comprises distearoyl phosphatidylcholine.

34. (Withdrawn) A method according to claim 23 further comprising adding a blowing agent to the feedstock.

35. (Withdrawn) A method according to claim 23 further comprising adding a polyvalent cation to the feedstock.

36. (Withdrawn) A method according to claim 23 wherein the feedstock is spray dried in a manner to produce particulates having a bulk density of less than 0.5 g/cm^3.

37. (Withdrawn) A pharmaceutical formulation prepared by a method according to claim 23.

38. (Currently Amended) A pharmaceutical formulation for pulmonary administration, the pharmaceutical formulation comprising:

particulates ~~comprising an~~ consisting essentially of active agent ~~amphotericin B particle~~ particles in a ~~lipid~~ matrix comprising a phospholipid, the active agent having a solubility in water of less than 1.0 mg/ml and wherein the active agent particles are dispersed throughout the phospholipid matrix; and

wherein at least 90% of the ~~amphotericin B~~ active agent particles ~~in the pharmaceutical formulation~~ have a geometric diameter less than 3 μm and wherein the particulates are hollow and/or porous, and have a mass median diameter less than 20 μm, a bulk density of less than about 0.5 g/cm^3 and a mass median aerodynamic

diameter less than about 2.6 μm.

39. (Currently Amended) A pharmaceutical formulation according to claim 38 wherein ~~the particulates have a mass median diameter less than 10 μm~~ the formulation provides for the delivery to the lung of a dose of at least about 5 mg in a single inhalation.

40. (Original) A pharmaceutical formulation according to claim 38 wherein the particulates have a mass median diameter less than 5 μm.

41. (Currently Amended) A pharmaceutical formulation according to claim 38 wherein ~~at least some of the particulates comprise a plurality of amphotericin B particles in a lipid matrix~~ a formulation fine particle fraction of less than 3.3 μm is at least about 72 percent.

42. (Currently Amended) A pharmaceutical formulation according to claim 38 wherein ~~the amphotericin B particles are crystalline~~ the formulation provides for the delivery to the lung of a dose of at least about 5 mg in a single inhalation.

43. (Cancelled).

44. (Currently Amended) A pharmaceutical formulation according to claim 38 wherein the ~~lipid~~ matrix comprises one or more of dipalmitoylphosphatidylcholine, ~~distearoylphosphatidylcholine~~ distearoylphosphatidylcholine, diarachidoylphosphatidylcholine dibehenoylphosphatidylcholine, diphosphatidyl glycerol, short-chain phosphatidylcholines, long-chain saturated phosphatidylethanolamines, long-chain saturated phosphatidylserines, long-chain saturated phosphatidylglycerols, and long-chain saturated phosphatidylinositols.

45-46 (Cancelled)

47. (Original) A pharmaceutical formulation according to claim 38 wherein the particulates have a bulk density less than 0.3 g/cm^3.

48. (Original) A pharmaceutical formulation according to claim 38 wherein the particulates have a bulk density less than 0.2 g/cm^3.

49. (Original) A pharmaceutical formulation according to claim 38 wherein the particulates are in dry powder form for aerosolization in a dry powder inhaler.

50. (Original) A pharmaceutical formulation according to claim 38 wherein the particulates are suspended in a propellant for aerosolization in a metered dose inhaler.

51. (Original) A pharmaceutical formulation according to claim 38 wherein the particulates are suspended within a liquid for aerosolization in a nebulizer.

52. (Original) A pharmaceutical formulation according to claim 38 wherein the particulates further comprise a polyvalent cation.

53. (Currently Amended) A pharmaceutical formulation according to claim 38 wherein the particulates are formed by spray drying with a blowing agent.

54. (Currently Amended) A pharmaceutical formulation for pulmonary administration, the pharmaceutical formulation comprising:

particulates comprising an amphotericin B particle in a ~~lipid~~ matrix comprising a phospholipid wherein the amphotericin B particles have a solubility in water of less than 1.0 mg/ml, and are dispersed throughout the phospholipid matrix, and;

wherein the particulates are hollow and/or porous and ~~wherein the particulates~~ have a mass median diameter less than 20 μm, a bulk density of less than about 0.5 g/cm^3 and a mass median aerodynamic diameter less than about 2.6 μm.

55. (Original) A pharmaceutical formulation according to claim 54 wherein the particulates have a mass median diameter less than 10 μm.

56. (Original) A pharmaceutical formulation according to claim 54 wherein the particulates have a mass median diameter less than 5 μm.

57. (Cancelled)

58. (Original) A pharmaceutical formulation according to claim 54 wherein the amphotericin B particles are crystalline.

59. (Cancelled)

60. (Currently Amended) A pharmaceutical formulation according to claim 54 wherein the lipid matrix comprises one or more of dipalmitoylphosphatidylcholine, ~~distearoylphosphatidylcholine~~ distearoylphosphatidylcholine, diarachidoylphosphatidylcholine dibehenoylphosphatidylcholine, diphosphatidyl glycerol, short-chain phosphatidylcholines, long-chain saturated phosphatidylethanolamines, long-chain saturated phosphatidylserines, long-chain saturated phosphatidylglycerols, and long-chain saturated phosphatidylinositols.

61. (Cancelled)

62. (Original) A pharmaceutical formulation according to claim 54 wherein the particulates have a bulk density less than 0.3 g/cm^3.

63. (Original) A pharmaceutical formulation according to claim 54 wherein the particulates have a bulk density less than 0.2 g/cm^3.

64. (Original) A pharmaceutical formulation according to claim 54 wherein the particulates are in dry powder form for aerosolization in a dry powder inhaler.

65. (Original) A pharmaceutical formulation according to claim 54 wherein the particulates are suspended in a propellant for aerosolization in a metered dose inhaler.

66. (Original) A pharmaceutical formulation according to claim 54 wherein the particulates are suspended within a liquid for aerosolization in a nebulizer.

67. (Original) A pharmaceutical formulation according to claim 54 wherein the particulates further comprise a polyvalent cation.

68. (Currently Amended) A pharmaceutical formulation according to claim 54 wherein the particulates are formed by spray drying with a blowing agent.

69- 83 (Cancelled).

84. (Withdrawn) A method of making a pharmaceutical formulation for pulmonary administration, the method comprising: suspending amphotericin B particles and a hydrophobic material in a liquid feedstock, wherein at least 90% of the active agent particles have a geometric diameter less than 3 μm; and spray drying the feedstock suspension to produce particulates comprising amphotericin B at least partially in the hydrophobic material.

85. (Withdrawn) A method according to claim 84 further comprising collecting the particulates, wherein the collected particulates have a mass median diameter less than 20 μm.

86. (Withdrawn) A method according to claim 84 further comprising collecting the particulates, wherein the collected particulates have a mass median diameter less than 10 μm.

87. (Withdrawn) A method according to claim 84 wherein the hydrophobic material comprises a lipid.

88. (Withdrawn) A method according to claim 84 wherein the hydrophobic material comprises a phospholipid.

89. (Withdrawn) A method according to claim 84 wherein the hydrophobic material comprises a hydrophobic amino acid.

90. (Withdrawn) A method according to claim 84 further comprising adding an emulsifying agent to the feedstock.

91. (Withdrawn) A method according to claim 84 further comprising adding a blowing agent to the feedstock.

92. (Withdrawn) A method according to claim 84 further comprising adding a polyvalent cation to the feedstock.

93. (Withdrawn) A method according to claim 84 wherein the feedstock is spray dried in a manner to produce particulates having a bulk density of less than 0.5 g/cm^3.

94. (Withdrawn) A pharmaceutical formulation prepared by a method according to claim 84.

95. (Withdrawn) A method of making a pharmaceutical formulation for pulmonary administration, the method comprising: suspending amphotericin B particles in a liquid feedstock, the liquid feedstock having a lipid and a blowing agent dissolved or suspended therein; and spray drying the feedstock suspension to produce hollow and/or porous particulates comprising amphotericin B and the lipid.

96. (Withdrawn) A method according to claim 95 further comprising collecting the particulates, wherein the collected particulates have a mass median diameter less than 20 μm.

97. (Withdrawn) A method according to claim 95 further comprising collecting the particulates, wherein the collected particulates have a mass median diameter less than 10 μm.

98. (Withdrawn) A method according to claim 95 wherein the lipid comprises a phospholipid.

99. (Withdrawn) A method according to claim 95 further comprising adding an emulsifying agent to the feedstock.

100. (Withdrawn) A method according to claim 95 further comprising adding a polyvalent cation to the feedstock.

101. (Withdrawn) A method according to claim 95 wherein the feedstock is spray dried in a manner to produce particulates having a bulk density of less than 0.5 g/cm^3.

102. (Withdrawn) A pharmaceutical formulation prepared by a method according to claim 95.

103. (New) A pharmaceutical formulation according to claim 1 wherein the active agent comprises ciprofloxacin.